Problem sheet 4

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Consider an empty one-dimensional domain, $[0, L]$, such that $x = 0$ is insulated. At time $t = 0$ the boundary $x = L$ is turned into a source of morphogen, M, of constant strength S. The morphogen is able to diffuse away from the boundary at a rate D and decays at a rate proportional to itself with constant of proportionality r.

1. Justify the following model of this set up,

$$\frac{\partial M}{\partial t} = D\frac{\partial^2 M}{\partial x^2} - rM, \quad 0 < x < L, \tag{1}$$

$$M(x, 0) = 0, \tag{2}$$

$$\frac{\partial M(0, t)}{\partial x} = 0, \quad M(L, t) = S. \tag{3}$$

2. Determine the steady state distribution, $M(x, t) = M_s(x)$.

Suppose the domain is filled with cells that are able to sense the concentration of M and that the cells can differentiate into two different forms based on the concentration of M that they sense. Namely, if $M_s < S/2$ then cells differentiate into form 1, whilst if $M_s > S/2$ then then cells differentiate into form 2. Define $x_s \in [0, L]$ to be the point which delineates the regions between cells of form 1 and cells of form 2.

3. Draw two sketches of $M_s(x)$ to show that x_s may, or may not exist.

4. Show that

$$x_s = \sqrt{\frac{D}{r}} \cosh^{-1}\left(\frac{1}{2}\cosh\left(\sqrt{\frac{r}{D}}L\right)\right). \tag{4}$$

5. Using equation (4) and the intuition from question 3, under what parameter conditions does x_s exist? Hint: the inverse of cosh does not output real values for all input values.

6. By sketching M_s for multiple values of L, suggest what happens to x_s as L gets larger.

7. Follow the proceeding steps derive a first order approximation of x_s in L, for large L.

   (a) Noting that:
   - $\cosh(x) = \frac{1}{2}(\exp(x) + \exp(-x))$;
   - $\cosh^{-1}(x) = \ln\left(x + \sqrt{x^2 - 1}\right)$.

   what is $\cosh\left(L\sqrt{r/D}\right)$ for large L?

   (b) Using the answer from part 7a show that, for large L,

$$x_s \approx \sqrt{\frac{D}{r}} \ln\left(\frac{1}{2}\exp\left(\sqrt{\frac{r}{D}}L\right)\right). \tag{5}$$

(c) Rearrange equation (5) to generate a form

$$x_s \approx L - C, \tag{6}$$

where C is a positive constant that should be defined.

8. Does solution (6) confirm the intuition gained from the question 6?

9. What does equation (6) mean for the cell populations on a large domain?

10. (Optional) Using computer software you are comfortable with plot equations (4) and (6) with values $D = 10$ and $r = 1$ for $0 \leq L \leq 10$. Be careful of where the solution becomes x_s becomes imaginary. How good is the approximation? Estimate the length, L, at which M_s is always above $S/2$.

1.1 Answers

1.

$$\underbrace{\frac{\partial M}{\partial t}}_{\substack{\text{Rate of change of} \\ \text{morphogen} \\ \text{concentration}}} = \underbrace{D\frac{\partial^2 M}{\partial x^2}}_{\substack{\text{Diffusion of} \\ \text{morphogen} \\ \text{through domain}}} - \underbrace{rM}_{\substack{\text{Decay of} \\ \text{morphogen}}} , \quad \underbrace{0 < x < L}_{\text{Domain size}} , \tag{7}$$

$$\underbrace{M(x,0) = 0}_{\text{Initial condition}} , \tag{8}$$

$$\underbrace{\frac{\partial M(0,t)}{\partial x} = 0}_{\substack{\text{Left boundary is} \\ \text{insulated}}} , \quad \underbrace{M(L,t) = S}_{\substack{\text{Right boundary is} \\ \text{a constant flux}}} . \tag{9}$$

2. Since we are looking for a steady state distribution we can set the time derivative to zero. We then look for solutions of the form

$$M_s = \exp(\lambda x) \tag{10}$$

and derive a condition for λ. However, in this case it is easier to look for solutions using the substitution

$$M_s = A\cosh(\lambda x) + B\sinh(\lambda x), \tag{11}$$

which is simply an alternate form of substitution (10). Critically, starting with the boundary condition at $x = 0$ we find that $B = 0$. Similarly, the boundary condition at $x = L$ provides us with

$$A = \frac{S}{\cosh(\lambda L)}. \tag{12}$$

Finally, substituting equation (11) into equation (1) and simplifying we generate

$$0 = D\lambda^2 - r. \tag{13}$$

Since cosh is a even function (*i.e.* $f(x) = f(-x)$) we only need to take the positive root. Thus,

$$M_s = \frac{S\cosh\left(\sqrt{\frac{r}{D}}x\right)}{\cosh\left(\sqrt{\frac{r}{D}}L\right)}. \tag{14}$$

3. See Figure 1. Key things to note, the plot is a cosh, so, it looks approximately exponential. We have to obey the boundary conditions, so the derivative is zero at $x = 0$ and the concentration is fixed at S at $x = L$. The final point to note depends on the level of M_s at $x = 0$. Depending how steep the gradient and how big L is x_s may, or may not, exist.

4. We want to find $x = x_s$ such that $M_s = S/2$. Substituting these values in,

$$\frac{S}{2} = \frac{S\cosh\left(\sqrt{\frac{r}{D}}x_s\right)}{\cosh\left(\sqrt{\frac{r}{D}}L\right)}. \tag{15}$$
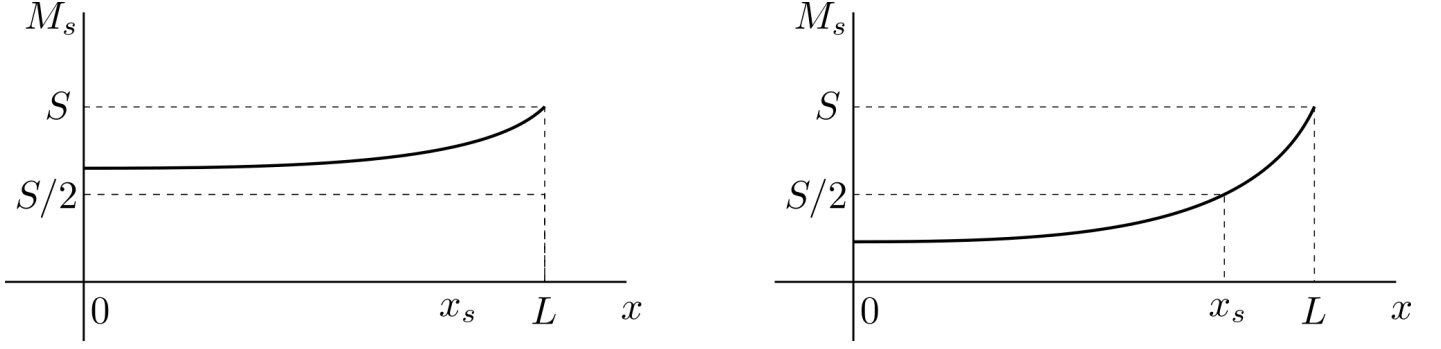
and rearranging gives equation (4).

2

Figure 1: Sketches of M_s and x_s. Note it is possible that the gradient is very shallow (left) and, thus, no x_s exists. However, if the gradient is steep enough (right) then x_s does exist.

5. $\cosh^{-1}(y)$ does not give real values for $y < 1$. Thus, for x_s to exist we require

$$\cosh\left(\sqrt{\frac{r}{D}}L\right) \geq 2. \tag{16}$$

This can be rearranged in various ways, but there is no real simpler presentation.

6. See Figure 2. As the domain size increases the population decays more and more. This can also be seen using inequality (16). Namely, if the inequality is not satisfied initially (red line in Figure 2) increasing L is one way to satisfy the inequality. Intuitively, the population is only produced at the boundary and decays everywhere else as it moves. As L increases x_s also increases.
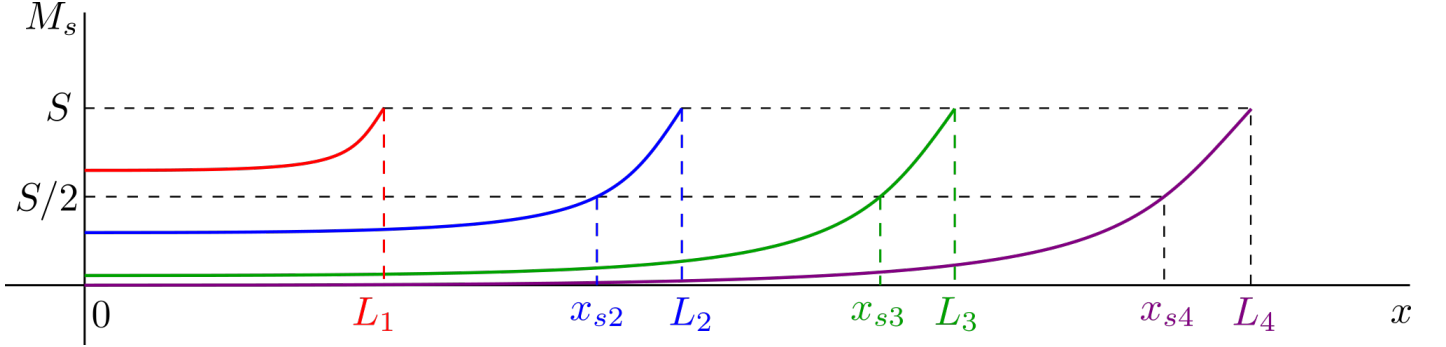

Figure 2: Sketches of M_s and x_s on increasingly larger domains.

7. For the following question

   (a) For $L \gg 1$ we have that $\cosh\left(L\sqrt{r/D}\right) \approx \exp\left(L\sqrt{r/D}\right)/2$.

   (b) Substituting this into the logarithmic form of $\cosh^{-1}$ we get

$$x_s = \sqrt{\frac{D}{r}}\cosh^{-1}\left(\frac{1}{2}\cosh\left(\sqrt{\frac{r}{D}}L\right)\right) \approx \ln\left(\frac{\exp\left(L\sqrt{r/D}\right)}{4} + \sqrt{\left(\frac{\exp\left(L\sqrt{r/D}\right)}{4}\right)^2 + 1}\right). \tag{17}$$

   Since $L \gg 1$

$$\sqrt{\left(\frac{\exp\left(L\sqrt{r/D}\right)}{4}\right)^2 + 1} \approx \frac{\exp\left(L\sqrt{r/D}\right)}{4}. \tag{18}$$

   So

$$x_s \approx \sqrt{\frac{D}{r}}\ln\left(\frac{\exp\left(L\sqrt{r/D}\right)}{2}\right) \tag{19}$$

3

(c) Expanding the logarithm in equation (19) provides

$$x_s \approx \sqrt{\frac{D}{r}} \left(\ln\left(\frac{1}{2}\right) + \ln\left(\exp\left(L\sqrt{r/D}\right)\right) \right), \tag{20}$$

which upon rearrangement and simplification gives

$$x_s \approx L - \sqrt{\frac{D}{r}} \ln(2). \tag{21}$$

8. Equation (21) tells us that x_s does indeed increase as L increases, it also tells us that x_s is (to a first order approximation) a constant distance, $C = \sqrt{D/r}\ln(2)$, away from the boundary $x = L$.

9. For large domains most of the cells are in form 1. Specifically, the only cells which see a concentration of morphogen above $S/2$ are those within the region $[L - C, L]$.

10. The plot can be seen in Figure 3. We see that the approximation becomes excellent for $L \geq 6$ and the solution of x_s disappears around $L \approx 4$.
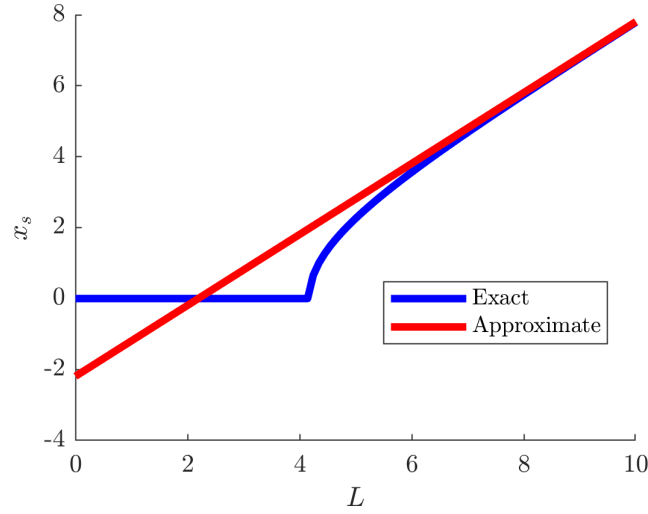

Figure 3: Comparing equations (4) and (6).

2 Patterning

Alongside the Schnakenberg system, which we have seen throughout the course, the Gierer-Meinhardt kinetics[1] are a well-known system of morphogen kinetics that produce Turing patterns.

The Gierer-Meinhardt reaction-diffusion system on a infinite one-dimensional domain is

$$\frac{\partial A}{\partial t} = f(A, H) + D_A \frac{\partial^2 A}{\partial x^2}, \tag{22}$$

$$\frac{\partial H}{\partial t} = g(A, H) + D_H \frac{\partial^2 H}{\partial x^2}, \tag{23}$$

where

$$f(A, H) = \frac{\rho_1 A^2}{(1 + KA^2) H} - \mu_1 A, \tag{24}$$

$$g(A, H) = \rho_2 A^2 - \mu_2 H. \tag{25}$$

where A and H are the morphogen populations and $K, \rho_1, \rho_2, \mu_1, \mu_2, D_A$ and D_H are positive constants. We assume that A and H remain finite over the domain and appropriate initial conditions are provided. **Initially, let us fix $K = 0$**.

As on sheet 2 this question is a good chance to practice deriving the Turing inequalities. However, if you are confident that you know what you are doing[2] then you can simply write down the required answers.

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[1]Meinhardt always maintained that the Schnakenberg system should be named after him and Gierer, as well, as it appeared as a specific case of one of their results in their original paper.

[2]Trust me, you don't.

1. $(0,0)$ is a homogeneous steady states of equations (22) and (23). What is the positive steady state, (A_s, H_s)?

2. Write down two inequalities that the positive steady state must satisfy in order to be stable, in the absence of diffusion.

3. Derive conditions under which the non-zero homogeneous steady state is stable in the absence of diffusion, but unstable when diffusion is included[3] (*i.e.* derive the Turing conditions).

Now assume that $K \neq 0$.

4. Show that the positive homogeneous steady state must satisfy

$$\frac{\mu_1 \rho_2 A_s}{\rho_1 \mu_2}(1 + K A_s^2) = 1. \tag{26}$$

5. Sketch the phase plane with nullclines $f = 0$ and $g = 0$ and demonstrate that there is still only one positive homogeneous steady state. Be sure to draw the two nullcline arrangements that can occur. Namely, the quadratic defined by $g = 0$ can cut $f = 0$ either before or after the maximum of $f = 0$. Do not forget to add the directional arrows specifying the signs of A_t and H_t.

6. What Jacobian sign structures are necessary for a Turing instability to take place?

7. Near the non-zero steady state the derivatives of (A_t, H_t) change sign. Use the nullcline plot to extract the signs of f_A, f_H, g_A and g_H and, thus, show that a diffusion-driven instability can occur in only one of the two situations. Hint: in a (A, H) phase plane the signs of f_A and g_A are defined by changes in signs of (A_t, H_t) along a horizontal path through (A_s, H_s), whereas the signs of f_H and g_H are defined by changes in the signs of (A_t, H_t) along a vertical path through (A_s, H_s).

2.1 Answers

1. Since we are looking for homogeneous steady states of equations (22) and (23), (A_s, H_s), we can ignore the spatial and temporal derivatives. Thus, the steady states are simultaneous solutions of $f(A_s, H_s) = g(A_s, H_s) = 0$,

$$0 = \frac{\rho_1 A_s^2}{H_s} - \mu_1 A_s, \tag{27}$$

$$0 = \rho_2 A_s^2 - \mu_2 H_s. \tag{28}$$

Ignoring the $(0,0)$ solution we can substitute equation (28) into equation (27) and derive

$$0 = \frac{\rho_1 \mu_2 A_s^2}{\rho_2 A_s^2} - \mu_1 A_s, \tag{29}$$

which provides a value for A. Substituting this back into equation (28) we are able to derive H_s. Thus, overall

$$(A_s, H_s) = \left(\frac{\mu_2 \rho_1}{\mu_1 \rho_2}, \frac{\mu_2 \rho_1^2}{\mu_1^2 \rho_2}\right). \tag{30}$$

2. To derive the stability criterion we need to derive the Jacobian of (f, g). This can be done by linearising around the positive steady state, *i.e.* substitute

$$\begin{pmatrix} A \\ H \end{pmatrix} = \begin{pmatrix} \frac{\mu_2 \rho_1}{\mu_1 \rho_2} \\ \frac{\mu_2 \rho_1^2}{\mu_1^2 \rho_2} \end{pmatrix} + \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix} \exp(\lambda t) \tag{31}$$

into the spatially homogeneous version of equations (22) and (23) and ignore quadratic and higher order terms of ϵ_1 and ϵ_2. We then finally derive conditions to ensure that the real part of λ is negative.

Alternatively, we can, straight away, write down the Jacobian

$$J(A, H) = \begin{bmatrix} 2\frac{\rho_1 A}{H} - \mu_1 & -\frac{\rho_1 A^2}{H^2} \\ 2 A \rho_2 & -\mu_2 \end{bmatrix} \tag{32}$$

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[3]As a personal hint I suggest keeping the system as $A_t = f(A, H) + D_A A_{xx}$ and $H_t = g(A, H) + D_H H_{xx}$, derive the inequalities in generality and then substitute the functional forms of f and g in at the end.

and evaluate it at the steady state

$$
J(A_s, H_s) = \begin{bmatrix} \mu_1 & -\frac{\mu_1{}^2}{\rho_1} \\ 2\frac{\mu_2\rho_1}{\mu_1} & -\mu_2 \end{bmatrix}.
\tag{33}
$$

Once again, we can derive the eigenvalues, λ, of $J(A_s, H_s)$ and derive conditions under which the eigenvalues have negative real parts.

Alternatively, we can check the notes in Appendix C and find that the stability criterion are

$$
0 > \text{trace}(J) = \mu_1 - \mu_2,
\tag{34}
$$

$$
0 < \det(J) = \mu_1\mu_2.
\tag{35}
$$

3. The first half of the problem (stability in the face of no diffusion) was done in the last question. Again you can either write the answers down from the notes, or derive them. Which is what we will do here. Since we are considering a spatial instability our perturbation is of the form

$$
\begin{pmatrix} A \\ H \end{pmatrix} = \begin{pmatrix} A_s \\ H_s \end{pmatrix} + \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix} \exp(\lambda t)\cos(kx).
\tag{36}
$$

Substituting perturbation (36) into equations (22) and (23) provides

$$
\lambda \exp(\lambda t)\cos(kx) \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix} = -k^2 \exp(\lambda t)\cos(kx) \begin{pmatrix} D_A & 0 \\ 0 & D_H \end{pmatrix} \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix} + \underbrace{\begin{pmatrix} f(A_s, H_s) \\ g(A_s, H_s) \end{pmatrix}}_{=0}
\tag{37}
$$

$$
+ \exp(\lambda t)\cos(kx) \begin{pmatrix} f_A & f_H \\ g_A & g_H \end{pmatrix} \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix}.
\tag{38}
$$

Rearranging and simplifying gives

$$
\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \begin{pmatrix} f_A - k^2 D_A - \lambda & f_H \\ g_A & g_H - k^2 D_H - \lambda \end{pmatrix} \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix}.
\tag{39}
$$

To have a non-trivial solution the matrix must have determinant zero,

$$
0 = \lambda^2 - \lambda(f_A + g_H - k^2(D_H + D_A)) + (f_A - k^2 D_A)(g_H - k^2 D_H) - f_H g_A.
\tag{40}
$$

To have an instability there must be at least one solution, λ, with positive real part. Since

$$
2\lambda_\pm = (f_A + g_H - k^2(D_H + D_A)) \pm \sqrt{(f_A + g_H - k^2(D_H + D_A))^2 - 4((f_A - k^2 D_A)(g_H - k^2 D_H) - f_H g_A)}
\tag{41}
$$

and we require $f_A + g_H < 0$ for stability in the absence of diffusion then we know that

$$
f_A + g_H - k^2(D_H + D_A) < 0
\tag{42}
$$

because $D_H + D_A > 0$. Thus, the only way to get to ensure $\lambda_+ > 0$ is to enforce

$$
0 > (f_A - k^2 D_A)(g_H - k^2 D_H) - f_H g_A = k^4 D_A D_H - k^2(D_A g_H + D_H f_A) + f_A g_H - f_H g_A = h(k^2).
\tag{43}
$$

Since h is a positive quadratic function in k^2 the only time it is negative is if there are two real, positive, roots:

$$
2D_A D_H k_\pm^2 = D_A g_H + D_H f_A \pm \sqrt{(D_A g_H + D_H f_A)^2 - 4D_A D_H(f_A g_H - f_H g_A)}.
\tag{44}
$$

Thus, to ensure $k_\pm^2$ are real and positive we require that

$$
D_A g_H + D_H f_A > 0,
\tag{45}
$$

$$
(D_A g_H + D_H f_A)^2 - 4D_A D_H(f_A g_H - f_H g_A) > 0,
\tag{46}
$$

$$
f_A g_H - f_H g_A > 0.
\tag{47}
$$

Since we already require $f_A g_H - f_H g_A > 0$ equations (45) and (47) can be wrapped up into

$$
D_A g_H + D_H f_A > 2\sqrt{D_A D_H(f_A g_H - f_H g_A)}.
\tag{48}
$$

Thus, finally, we can insert the functions f and g into the appropriate inequalities and specify that Turing patterns are generated when

$$
0 > \mu_1 - \mu_2,
\tag{49}
$$

$$
0 < \mu_1\mu_2,
\tag{50}
$$

$$
2\sqrt{D_A D_H \mu_1\mu_2} < D_H\mu_1 - D_A\mu_2.
\tag{51}
$$

4. Since we are looking for homogeneous steady states of equations (22) and (23), (A_s, H_s), we can ignore the spatial and temporal derivatives. Thus, the steady states are simultaneous solutions of $f(A_s, H_s) = g(A_s, H_s) = 0$,

$$0 = \frac{\rho_1 A_s^2}{(1 + KA_s^2) H_s} - \mu_1 A_s, \tag{52}$$

$$0 = \rho_2 A_s^2 - \mu_2 H_s. \tag{53}$$

Ignoring the $(0, 0)$ solution we can substitute equation (53) into equation (52) and derive

$$0 = \frac{\rho_1 \mu_2 A_s^2}{(1 + KA_s^2) \rho_2 A_s^2} - \mu_1 A_s, \tag{54}$$

which upon further manipulation gives equation (26).

5. The A nullclines are

$$A = 0, \tag{55}$$

$$H = \frac{\rho_1 A}{(1 + KA^2) \mu_1}. \tag{56}$$

The H nullcline is

$$H = \frac{\rho_2}{\mu_2} A^2. \tag{57}$$

The accompanying phase planes are shown in Figure 4. The figure demonstrates that there is one positive steady state.
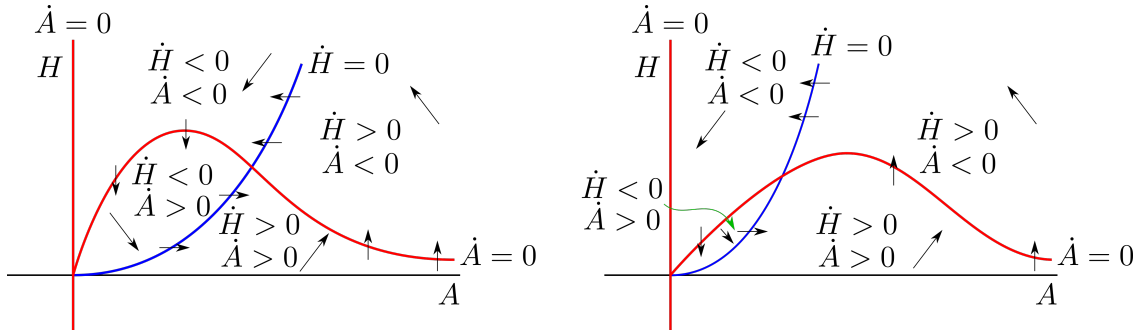

Figure 4: The Gierer-Meinhardt phase planes.

6. Either from looking it up from the notes, or deriving it from question 3. The Jacobian must have the sign form

$$\begin{bmatrix} + & + \\ - & - \end{bmatrix}, \quad \text{or} \quad \begin{bmatrix} + & - \\ + & - \end{bmatrix} \tag{58}$$

along with column and row permutations.

7. Consider Figure 5(a) which shows the nullcline arrangement where $\dot{H} = 0$ is to the right of the maximum of $\dot{A} = 0$. Focus on the steady state and consider travelling along the dashed line from x to x'. At x $\dot{A} = f > 0$ and at x' $\dot{A} = f < 0$, so as A increases $\dot{A} = f$ goes from positive to negative, so $\dot{A} = f$ must be a decreasing function of A near the steady state. This means that $f_A < 0$. Similarly at x, $\dot{H} = g < 0$ and at x', $\dot{H} = g > 0$, so as A increases $\dot{H} = g$ goes from negative to positive, so $\dot{H} = g$ must be an increasing function of A near the steady state. This means that $g_A > 0$. Following this logic along the vertical branch, from y to y' we discover that $f_H < 0$ and $g_H < 0$. Thus the accompanying Jacobian sign structure is

$$\begin{bmatrix} - & - \\ + & - \end{bmatrix} \tag{59}$$

and, so, a Turing instability cannot happen.

If we now consider Figure 5(b) which shows the nullcline arrangement where $\dot{H} = 0$ is to the left of the maximum of $\dot{A} = 0$. We see that travelling from x to x' and y to y' only ever takes us between two sectors. The same logic
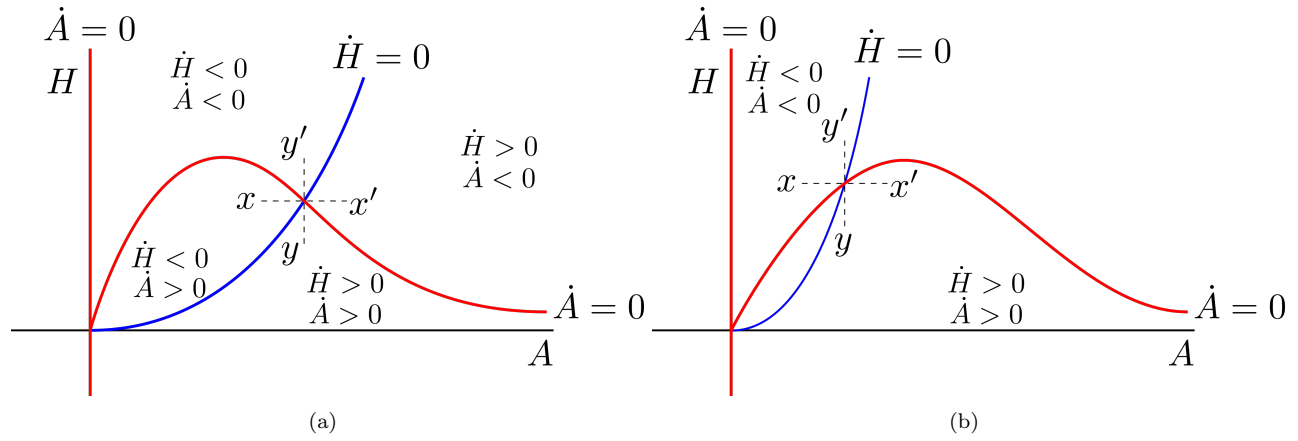
Figure 5: Extracting derivatives signs from the Geirer-Meinhardt phase planes.

applies and we can derive that $f_A > 0$, $f_H < 0$, $g_A > 0$ and $g_H < 0$. Thus the accompanying Jacobian sign structure is

$$\begin{bmatrix} + & - \\ + & - \end{bmatrix} \tag{60}$$

and, so, a Turing instability could happen.

3 Simulating Turing patterns

No Matlab this time. Simulating partial differential equations is not a simple task. However, there are websites out there that have done the heavy lifting for you.

The Gray-Scott reaction-diffusion model is

$$\frac{\partial u}{\partial t} = D_u \nabla^2 u - uv^2 + F(1 - u), \tag{61}$$

$$\frac{\partial v}{\partial t} = D_v \nabla^2 v + uv^2 - (F + k)v, \tag{62}$$

where appropriate boundary and initial conditions are assumed to be given and D_u, D_v, F and k are constants. F is known as the feed rate as it causes more u to be added to the system. k is the death rate as it controls the rate at which v is removed from the system.

You can play around with the feed rate, death rate and initial conditions through this online applet. What patterns can you create? As a base level try and find spots, labyrinthine patterns and constantly evolving patterns, like those shown in Figure 6. For those more adventurous try and find other patterns contained within these equations.

Exam Revision

4 Properties of Turing patterns

Consider a two species reaction-diffusion system with Neumann boundary conditions on a domain B, which has boundary ∂B,

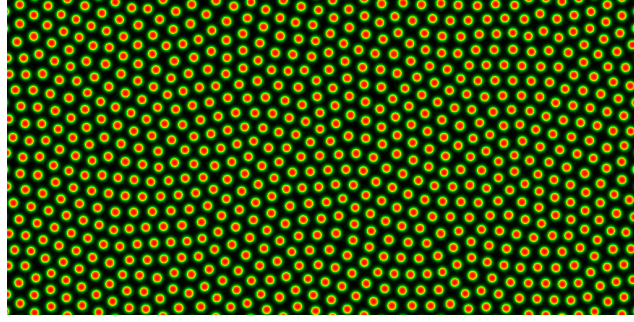$$\frac{\partial u}{\partial t} = D_u \nabla^2 u + f(u, v), \tag{63}$$

$$\frac{\partial v}{\partial t} = D_v \nabla^2 v + g(u, v), \tag{64}$$

$$\frac{\partial u}{\partial n} = \frac{\partial v}{\partial n} = 0 \text{ on } \partial B. \tag{65}$$
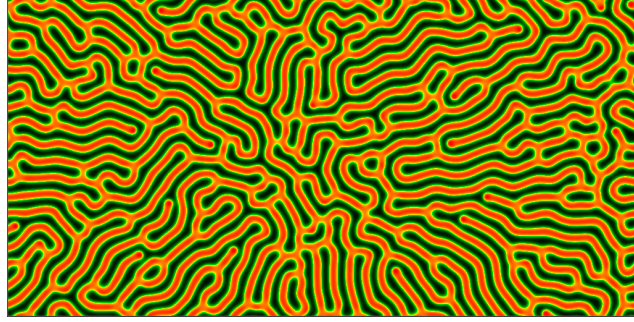
and random initial conditions. Further, assume that the kinetics and diffusion parameters are chosen such that the populations (u, v) undergo Turing patterning.

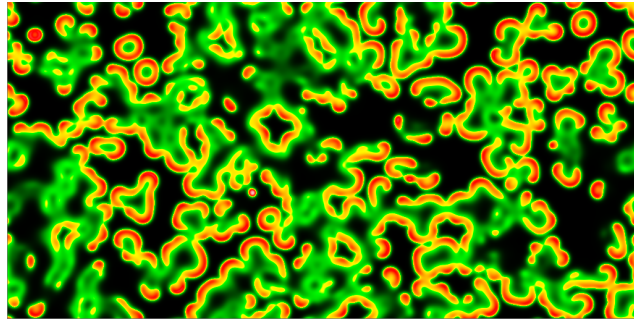1. Specify the Jacobian structures behind "cross" and "pure" kinetics.

Figure 6: Possible patterns in the Gray-Scott equations (61) and (62).

2. Explain why the resulting morphogen patterns of (u, v) are in phase when pure kinetics are used and out of phase when cross kinetics are used. Note: *in phase* means that the peaks and troughs of u and v occur at the same positions, where as *out of phase* means that the peaks of u correspond to the troughs of v and vice-versa. Hint: consider the signs of ϵ_1 and ϵ_2. Under what conditions are they the same/different? What does this mean?

3. Explain why spatial oscillations can never occur at a Turing bifurcation point. Namely, show that the unstable eigenvalue λ must always be real at the onset of patterning.

4. Why must $D_u \neq D_v$? (Hint: assume they are equal and derive a contradiction).

4.1 Answers

1. The "cross" kinetic Jacobian structure is

$$J = \begin{bmatrix} + & + \\ - & - \end{bmatrix}. \tag{66}$$

The "pure" kinetic Jacobian structure is

$$J = \begin{bmatrix} + & - \\ + & - \end{bmatrix}. \tag{67}$$

Note row and column permutations of the above are also valid.

9

2. We consider perturbations to the steady of the form

$$\begin{pmatrix} u \\ v \end{pmatrix} = \begin{pmatrix} u_s \\ v_s \end{pmatrix} + \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix} \exp(\lambda t) \tag{68}$$

where λ is an eigenvalue of

$$J - Dk^2 = \begin{pmatrix} f_u - k^2 D_u & f_v \\ g_u & g_v - k^2 D_v \end{pmatrix} \tag{69}$$

and

$$\boldsymbol{\epsilon} = \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix} \tag{70}$$

is a corresponding eigenvalue, thus,

$$(J - Dk^2)\boldsymbol{\epsilon} = \lambda\boldsymbol{\epsilon} \implies (J - Dk^2 - \lambda I)\boldsymbol{\epsilon} = 0. \tag{71}$$

Consider the case of cross kinetics and write down the signs we know in the matrix $(J - Dk^2 - \lambda I)$,

$$J - Dk^2 - \lambda I = \begin{pmatrix} ? & + \\ - & - \end{pmatrix}. \tag{72}$$

Namely, the top right and bottom left entries are just f_v and g_u, respectively, and, thus, do not change sign. The top left entry is positive (from f_u), but has values subtracted from it $(-k^2 D_u - \lambda)$, so we cannot guarantee its sign. However, the bottom right entry of J is negative $(g_v < 0)$ in the case of cross kinetics and since we are subtracting further values from it, the bottom right term of $J - Dk^2 - \lambda I$ remains negative.

Knowing these signs and that equation (71) must be satisfied we know that ϵ_1 and ϵ_2 must satisfy

$$\begin{pmatrix} s_1^? & s_2^+ \\ s_3^- & s_4^- \end{pmatrix} \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix} = 0, \implies \begin{array}{l} s_1^? \epsilon_1 + s_2^+ \epsilon_2 = 0, \\ s_3^- \epsilon_1 + s_4^- \epsilon_2 = 0, \end{array} \tag{73}$$

where s_j^i is some real number with sign i. The equation with unknown sign does not help. However, rearranging the other equation leads to

$$\frac{\epsilon_1}{\epsilon_2} = -\frac{s_3^-}{s_4^-}. \tag{74}$$

Since s_3^- and s_4^- are both negative the right-hand side of equation (74) is negative, thus, we deduce that ϵ_1 and ϵ_2 must be of opposite sign. Finally, without loss of generality, let $\epsilon_1 > 0 > \epsilon_2$ this means that the perturbation to u_s is a positive cosine, whilst the perturbation to v_s is a negative cosine and, thus, the patterns are out of phase.

The above logic can be followed with the pure kinetic sign structure. However, in this case you should derive that

$$\begin{pmatrix} s_1^? & s_2^- \\ s_3^+ & s_4^- \end{pmatrix} \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \end{pmatrix} = 0, \implies \begin{array}{l} s_1^? \epsilon_1 + s_2^- \epsilon_2 = 0, \\ s_3^+ \epsilon_1 + s_4^- \epsilon_2 = 0, \end{array} \tag{75}$$

resulting in

$$\frac{\epsilon_1}{\epsilon_2} = -\frac{s_3^+}{s_4^-}. \tag{76}$$

The right-hand sign on equation (76) is positive, meaning that ϵ_1 and ϵ_2 are the same sign. Thus, the perturbations to the steady states are in phase.

3. The eigenvalues of the Turing instability are

$$2\lambda_\pm = (f_u + g_v - k^2(D_u + D_v)) \pm \sqrt{(f_u + g_v - k^2(D_v + D_u))^2 - 4((f_u - k^2 D_u)(g_v - k^2 D_v) - f_v g_v)}. \tag{77}$$

These are imaginary if and only if

$$(f_u + g_v - k^2(D_v + D_u))^2 - 4((f_u - k^2 D_u)(g_v - k^2 D_v) - f_v g_v) < 0 \tag{78}$$

However, $(f_u + g_v - k^2(D_v + D_u))^2 > 0$ and for an instability to exist we need $-4((f_u - k^2 D_u)(g_v - k^2 D_v) - f_v g_v) > 0$. Thus, at the onset of patterning inequality (78) cannot be satisfied and, thus, $\lambda_\pm$ are real, so oscillations in time do not happen.

4. Two of the Turing inequalities are

$$f_u + g_v < 0 \tag{79}$$

$$D_v f_u + D_u g_v > 0. \tag{80}$$

If $D_v = D_u > 0$ then we could factor the constant out of equation (80) and, thus, be able to derive

$$f_u + g_v < 0 \tag{81}$$

$$f_u + g_v > 0, \tag{82}$$

resulting in a contradiction.

5 Creating the model

For each of the following images in Figure 7 write down a set of reaction-diffusion equations that could provide the images as a steady state solution. Do not forget to provide boundary conditions. For initial conditions assume that there is a small spatially random amount of morphogen throughout the domain.

Figure 7: Three steady state morphogen profiles.

5.1 Answers

Note that the following suggestions are non-unique (as illustrated in case 2), so if you have a different suggestion you could be right.

1. Things to notice:

   - the boundaries are fixed to two different values;
   - the profile of u decays away from the boundaries.

   Using these two pieces of information the follow reaction-diffusion equation should give a steady profile similar to Figure 7(a), for appropriate values of D and γ.

   $$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} - \gamma u, \tag{83}$$

   $$u(0,t) = S, \quad u(L,t) = S/2. \tag{84}$$

2. Since the entire profile is flat the boundaries could either be fixed at $S = 0$, or they could be zero-flux. One potential equation behind this system is:

   $$\frac{\partial u_1}{\partial t} = D\frac{\partial^2 u_1}{\partial x^2}, \tag{85}$$

   $$u_1(0,t) = S, \quad u_1(L,t) = S. \tag{86}$$

   Another potential is

   $$\frac{\partial u_2}{\partial t} = D\frac{\partial^2 u_2}{\partial x^2} + ru_2(S - u_2), \tag{87}$$

   $$\frac{\partial u_2}{\partial x}(0,t) = 0 = \frac{\partial u_2}{\partial x}(L,t). \tag{88}$$

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3. We note that the steady state is a combination of two heterogeneous morphogens that are out of phase. This suggests using a reaction-diffusion system. Equally, the morphogen profile at the boundaries is 'flat', which suggests zero-flux boundary conditions. Hence, we need a system of the following form

$$\frac{\partial u}{\partial t} = D_u \frac{\partial u}{\partial x} + f(u, v), \tag{89}$$

$$\frac{\partial v}{\partial t} = D_v \frac{\partial v}{\partial x} + g(u, v), \tag{90}$$

$$\frac{\partial v}{\partial x}(0, t) = \frac{\partial u}{\partial x}(0, t) = 0 = \frac{\partial u}{\partial x}(L, t) = \frac{\partial v}{\partial x}(L, t), \tag{91}$$

such that f and g satisfy the Turing instability inequalities (see equations (45) and (47)). Additionally, because the populations are out of phase we know that the Jacobian of partial derivatives must satisfy the cross kinetic pattern,

$$J = \begin{bmatrix} + & + \\ - & - \end{bmatrix}. \tag{92}$$

If you had gotten this far I would be happy with this answer. However, pushing your memory a little further you might remember that the Schnakenberg kinetics are Turing unstable and produce out of phase patterns and, thus, would make a satisfactory choice for f and g.